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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	**PAPER NUMBER**
1648	

NOTIFICATION DATE	DELIVERY MODE
03/15/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/665,975	**Applicant(s)** TAMM ET AL.	
	Examiner Agnieszka Boesen	**Art Unit** 1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 February 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *40,47 and 48*.
   Claim(s) withdrawn from consideration: *9, 10, 35-39, 41-46, and 49-57*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Response to arguments

The Amendment filed February 26, 2007 is acknowledged and entered.

Election/Restriction

Applicant argues that claims 9, 10, 35-39, 41-46, and 49-57, drawn to siRNA compounds should not have been withdrawn in the Final office action of October 24, 2006, but should have been examined together with claims 40, 47, and 48 drawn to antibody compounds. Applicant requests withdrawal of Finality and issuance of a new action.

In the Final Office action of October 24, 2006, claims 9, 10, 35-39, 41-46, and 49-57 were withdrawn because the claims were directed to an invention independent or distinct from the invention originally claimed. The original claims 9 and 10 were broadly drawn to any compounds that inhibit anti-apoptotic activity of Survivin. In the restriction requirement of December 13, 2005, examiner grouped claims 9 and 10 in one group III, drawn to a compound that inhibits Survivin. No election of species for group III was made because claims 9 and 10 did not recite any species. Thus Examiner could not have made a species election requirement or could not have grouped the distinct compounds into different groups because no specific compounds were recited in claims 9 or 10. Applicant elected group III for examination on the merits. Examiner went to Applicant's specification and found that compounds that inhibit anti-apoptotic activity of Survivin can include antibodies, small molecules, peptidomimetics, antisense nucleic acids or siRNA. Examiner made art rejections under 35 USC § 102(b) for the antibody compounds. In the supplemental response of August 22, 2006 Applicant amended claim 9 to recite a specific compound such as siRNA, which was not rejected in the First Office action of February 22, 2006.

Applicant argues that Applicant did not constructively elect to prosecute claims relating to antibodies and that Applicant could not have received an action on the merits relating to polyclonal antibodies, as no such antibody claims were pending. However because claims 9 and 10 did not specify what compounds may inhibit Survivin, Examiner went for guidance to the specification and found that such compounds could be antibodies. Thus Examiner performed a search for antibodies, and made an art rejection. Applicant argues that the Examiner should have searched the entire genus of compounds. Examiner respectfully disagrees. It would have been an undue burden for the Office to search all possible molecules such as small molecules, peptidomimetics, antisense nucleic acids or siRNA that inhibit Survivin. If the specific species of inhibitory compounds had been recited in the claims, a species election requirement would have been made by the Examiner. However because the species were not recited in the claims, examination was based on the guidance provided in the specification. The species examined was an antibody and was sufficient to reject the generic claims.

The MPEP 803.02 states: "Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration." In the present case no election of species was required or made because claims 9 and 10 did not recite species. Thus, examination was based on the guidance provided in the specification. The species examined was an antibody. The species of an antibody is not currently allowable and thus examination is limited to the examined

species. For this reason the claims drawn to species patentably distinct from the examined species, such as siRNA are withdrawn from further consideration. The restriction is deemed proper and is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 40, 47, and 48 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is maintained**. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that the specification clearly describes a representative number of species of compounds through its full description of antisense compounds, siRNA compounds and antibodies, which inhibit the anti-apoptotic activity of Survivin. Applicant also argues that although Applicants did not provide a specific working example of using small molecules to inhibit the anti-apoptotic activity of Survivin, such example is clearly not required according to Federal Circuit (see *Falkner v. Inglis*). Examiner points out that in the *Falkner v. Inglis* case the molecule in question was not a small molecule compound but DNA. A small molecule compound is typically considered in the art to be a chemical compound such as for example NSAID drugs. In a different case in which small molecule compounds are actually in question, the Federal Circuit

court held that without a disclosure of specific molecules that can in fact inhibit a activity of the PGHS-2 the claimed methods couldn't be said to have been described." See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described."). Thus with regard to small molecule compounds, the disclosure of a particular structure was required to satisfy a written description requirement. In the present case the structures of compounds that inhibit the interaction of Survivin with HBXIP are essential for the purpose of the current invention and are required to satisfy the written description requirement.

Although reduction to practice and working examples may not always be required to show possession and to satisfy the written description requirement, the specification should disclose specific structures of compounds which function is being claimed. A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)).

An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed.

Applicant argues that the specification describes a multitude of species including antibodies, small molecules, peptidomimetics, antisense nucleic acids and siRNA compounds that demonstrate to one of ordinary skill in the art that Applicants were in full possession of the genus of isolated compounds that inhibit HBXIP. Examiner respectfully disagrees. Each class of compounds, such as antibodies, small molecules, peptidomimetics, antisense nucleic acids and siRNA, dislosed in the specification, represents another broad genus within the genus of generic compounds claimed to inhibit the activity of Survivin. Applicant is required to provide a representative number of species within each claimed genus: 1) a genus of small molecules, 2) a genus of peptidomimetics, 3) a genus of antisense nucleic acids and siRNA, and 4) a genus of antibodies.

The mere contemplation of the claimed genus in the specification is not sufficient to support the presently claimed invention directed to a genus of antibodies and siRNA molecules. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical

properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406."

A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. See MPEP 2105.

The skilled artisan cannot envision the detailed structure of a genus of compounds that are contemplated in the invention. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed

invention as presently claimed. For the reasons discussed above the current rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 40 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Banks et al. ("Survivin does not inhibit caspase –3 activity" Blood, 2000) **is maintained.**

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that the reference does not directly teach an antibody that binds Survivin and inhibits its binding to HBXIP and that Examiner must be relying on the fact that such as antibody would inherently provide the recited effect of reducing the activity of HBXIP. Applicant argues that to establish inherency the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. Applicant argues that it would have been unexpected for Bank's antibody to bind the exact epitope of a native folded form of Survivin, because Bank's antibody was used in a Western Blot involving denaturation of protein sample.

However, because Bank's antibody does bind Survivin and because the claims are drawn to a genus of antibodies that interfere with Survivin binding to HBXIP, and not a specific antibody structure, the reference antibody is expected to inhibit the anti-apoptotic activity of

Survivin. The fact that the Bank's antibody was used in a Western Blot does not play a role, because, either in the acrylamid gel or in a tissue/cell, the structure of Survivin is still the same, i.e., all the epitopes of Survivin are present in the gel. If the antibody designed to detect native from of Survivin was not binding the Survivin in the polyacrylamide gel that antibody would have been useless. Thus the antibody that binds Survivin in the gel is expected to bind the native form of the Survivin. For the reasons discussed above the rejection is maintained.

Rejection of claims 40, 47, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Yagihashi et al. ("Detection of Anti-Survivin Antibody in gastrointestinal cancer patients" Clin Chem, 2001) **is maintained.**

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that Yagihashi does not describe an *isolated compound* comprising a polyclonal antibody as recited in independent claims 40, because Yagihashi used *human sera* in an ELISA assay to detect whether a patient made antibodies against Survivin. Examiner would like to point out that the dependent claim 48 is drawn to the *isolated compound* wherein the antibody comprises a *polyclonal antibody*. Applicant's argument is contradictory to what is claimed in claim 48. Applicant argues that the antibodies *were not isolated* from the sera. Because the antibodies were obtained from a patients sera and used to detect Survivin in an ELISA assay the antibodies are considered to have been isolated. Applicant argues that the polyclonal antibody from human sera used to bind Survivin in an ELISA assay, would not bind the native form of Survivin. Examiner respectfully disagrees. Obviously Yagihashi intended to detect if the patient had antibodies to the native form of Survivin, and the fact that the patient made the antibodies against Survivin, those

antibodies they are binding the native form of Survivin. Yagihashi has shown that the human sera contained polyclonal antibodies binding Survivin. Those antibodies are expected to inhibit the interaction of Survivin with HBXIP. For the reasons discussed above the current rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AB

Agnieszka Boesen

3/8/2007

Stacy B. Chen 3/8/07

STACY B. CHEN
PRIMARY EXAMINER